Biochip with Cu-Graphene Glassy Carbon Electrode for Glucose Sensing

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Abstract

Diabetes has become a serious global health threat and glucose test is very important for diabetic patients on a daily basis. Traditional blood glucose test uses a lancet device to prick the patient's finger to get a drop of blood sample for testing. This invasive test causes pain to patient and increases the risk of cross-infection of blood-transmitted diseases. Non-invasive glucose monitoring has become very attractive alternative to blood glucose test. Research has found that other biological samples (e.g. saliva, tears, sweat, urine) also contains trace amount of glucose molecules and they may be used for diabetes diagnosis. However, glucose level in such biological samples is generally too low for traditional sensors. Nanotechnology offers new hope in high-resolution glucose sensing. In this research, we proposed a saliva glucose sensor that combines graphene-based glucose nanosensor with microfluidic biochip to develop a complete lab-on-a-chip (LoC) system for non-invasive glucose sensing. It is designed to collect, prepare and manipulate the microfluidic sample for glucose sensing using graphene-based glucose nanosensor. The key components of the lab-on-a-chip are designed and simulated with COMSOL. The LoC device may be used for non-invasive glucose sensing for diabetes diagnosis and self-monitoring.

Introduction

According to 2014 World Health Organization report, about 347 million people worldwide have diabetes. Diabetes is predicted to become the 7th leading cause of death in the world by the year 2030. US Center for Disease Control and Prevention (CDC) estimates more than 29 million people - or 9.3% of the US population - to have diagnosed or undiagnosed diabetes. More than 200,000 deaths occur each year among people with diabetes in the United States. Diabetes has become serious threat to public health and there is urgent need for diabetes prevention and health management worldwide.

Diabetic patients need to monitor their blood glucose level in daily basis to adjust medication or insulin usage. Traditional blood glucose test uses a lancet device to prick the patient's finger to get a drop of blood sample for testing. This invasive test causes pain to patient and increases the risk of cross-infection of blood-transmitted diseases. Non-invasive glucose monitoring has become very attractive alternative to blood glucose test. Research has found that saliva glucose is promising to be used as biological sample for diabetes diagnosis. However, the major challenging in the testing is that the glucose concentration in saliva is generally very low and many other ingredient in saliva may interfere with the measurement. To overcome this issue, graphene offers the opportunity to alternative saliva for non-invasive painless glucose sensing due to their extremely large surface area and improved catalytic activities even in the molecular level. In this research, we proposed a saliva glucose sensor that combine graphene-base glucose nanosensor with microfluidic biochip to develop a complete lab-on-chip (LoC) system for non-invasive glucose sensing using saliva sample. As shown in Figure 1, the proposed biochip takes the sample to be tested, performs necessary on-chip sample preparation and manipulation, and drives it toward the reacting chamber for electrochemical glucose sensing. The Cu nanoparticle and graphene sheets are pre-deposited on the working electrode to enable highly selective and sensitive detection of minute glucose concentration in the sample. The electrochemical current can be measured by a signal sensing circuitry, and converted into corresponding glucose concentration to be read on a LCD display.

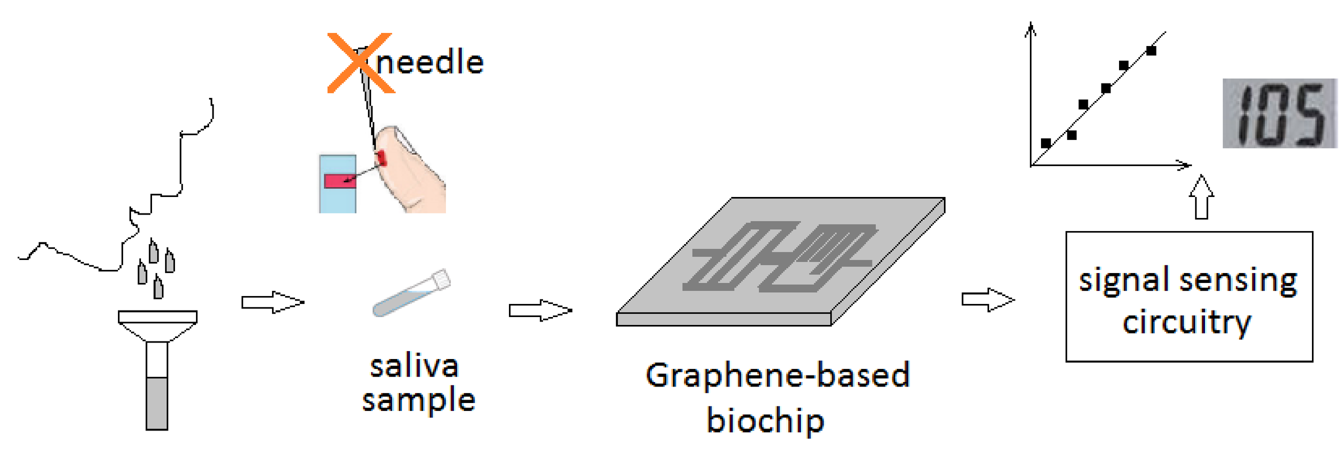


Figure 1. Non-invasive glucose sensing using saliva sample

The aimed device does not cause any wound to patient's body and avoids cross-infection of blood-transmitted diseases during the testing. It may allow continuous monitoring of glucose level, which is very important for diabetes patients in their disease self-monitoring. With the measured glucose level, diabetic patients can adjust their medication intake or insulin injection to achieve healthy control of the disease.

Design and Working Principle

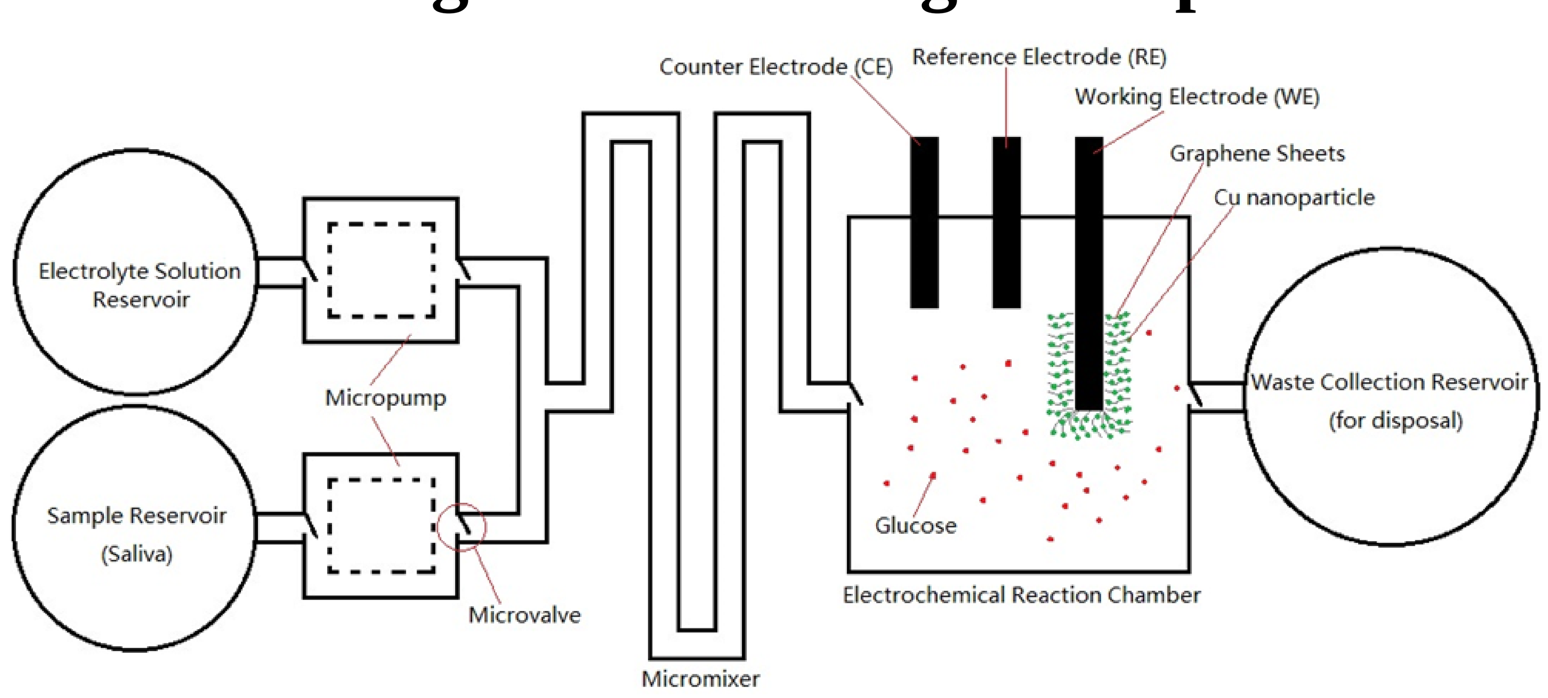


Figure 2. Biochip with graphene-based nanosensor for non-invasive glucose sensing

The proposed lab-on-a-chip with graphene-based nanosensor for non-invasive glucose sensing is shown in Figure 1. It consists of three functional stages: sample preparation, electrochemical sensing chamber, and waste disposal. It also consists of two electrolyte solution reservoirs for storing electrolyte solutions and saliva sample; two micropumps for pumping the electrolyte solution and saliva samples into the following micromixer; the microvalves for regulating the direction of the microfluidic flow; the micromixer for improving the mixing. Once electrolyte solution and saliva samples are thoroughly mixed, they are injected into the electrochemical reaction chamber. There are three electrodes pre-embedded in the chamber: Counter Electrode (CE), Reference Electrode (RE) and Working Electrode (WE) with graphene and Cu nanoparticles pre-deposited on its surface. The glucose concentration in the saliva sample can be derived by measuring the electrochemical current between the electrodes when glucose molecules in saliva interact with Cu nanoparticle in graphene sheets and changes the electrocatalytic activities. After the glucose level is identified, the mixed solution is pumped into waste collection reservoir for disposal.

The preparation of the Cu modified graphene (Cu-graphene) electrode mainly refers to Jing Luo's method [J. Luo, et al, Analytica Chimica Acta, 2012]. The working principle of the Working Electrode (WE) with graphene and Cu nanoparticles is explained as below. Free electrons are produced during the Reduction-Oxidation. Once chamber, the current is then converted into corresponding glucose concentration.

Preparation and Evaluation of the Cu-Graphene Glassy Carbon Electrode

The preparation and Evolution of the Cu-Graphene Glassy Carbon (GC) Electrode includes three steps: firstly, prepare Glass Carbon (GC) electrode; secondly, prepare of Graphene electrode; thirdly, prepare of Cu-Graphene electrode. In addition, Cyclic Voltammetry (CV) is an electrochemical technique which measures the current that develops in an electrochemical cell under conditions where voltage is in excess of that predicted by the Nernst equation. CV is performed by cycling the potential of a working electrode, and measuring the resulting current. A cyclic voltammogram is obtained by measuring the current at the working electrode during the potential scans. It shows a cyclic voltammogram resulting from a single electron reduction and oxidation. In this project, CV is used to study qualitative information about electrochemical processes under various given conditions, and evaluate the performance of the Cu-Graphene GC electrode.

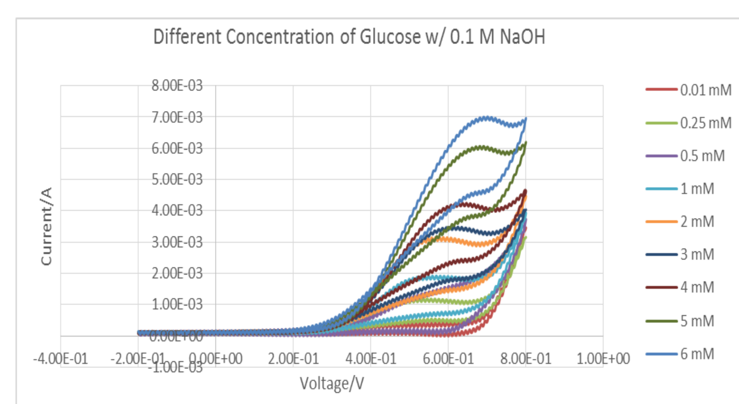
1. Preparation of Graphene electrode:

Method 1: Using graphene powder:
- a very small amount of graphene powder;
- form a thin film on DI water;
- insert the GC electrode for several minutes;
- take electrode out and dry in room temperature.

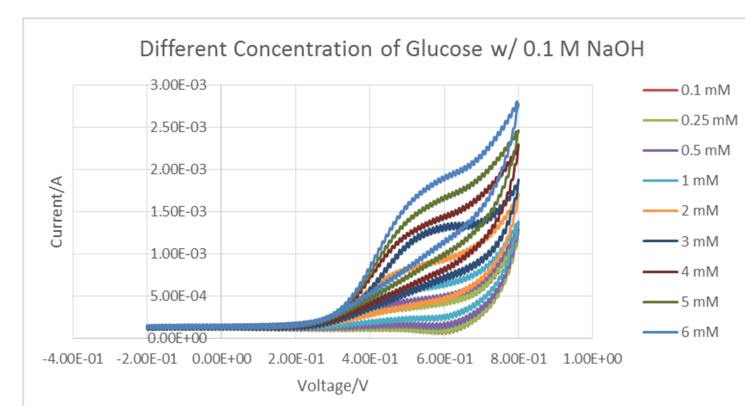
Method 2: Use Graphene dispersion:
- 1.5mg/mL;
- a certain droplet onto the surface of the GC electrode;
- dry in room temperature.

2. Preparation of Cu-Graphene electrode

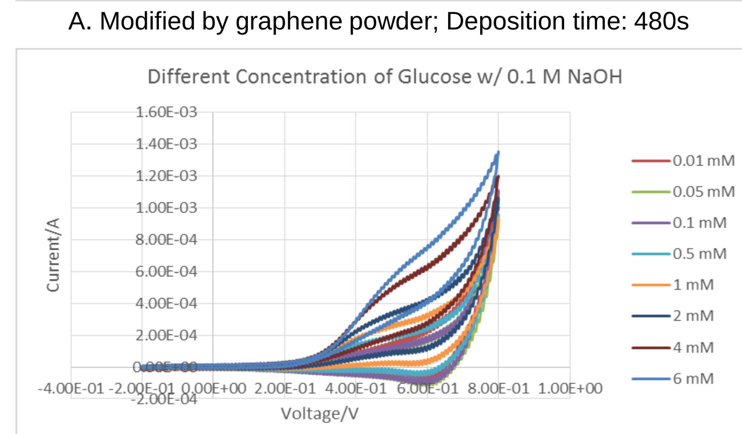
For deposition of Cu nanoparticle:
- Cu Source: CuSO4;
- Solution: 10 mM $CuSO_4$ and 100 mM Na_2SO_4;
- Deposition time: 480s (8 mins)
  960s (16 mins)
  1440s (24 mins)



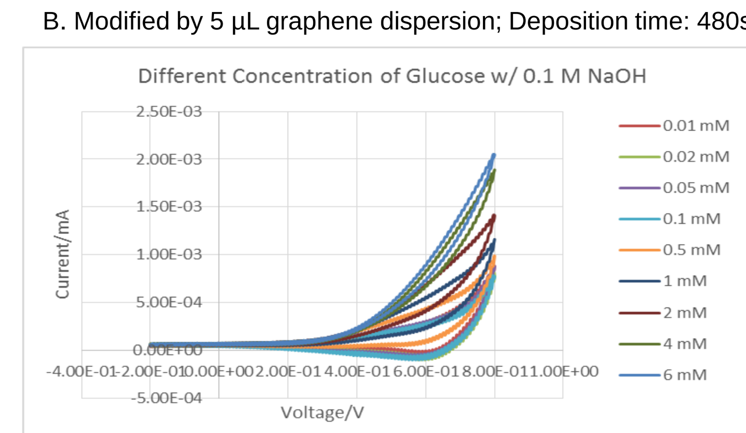
A. Modified by graphene powder; Deposition time: 480s



B. Modified by 5 µL graphene dispersion; Deposition time: 480s

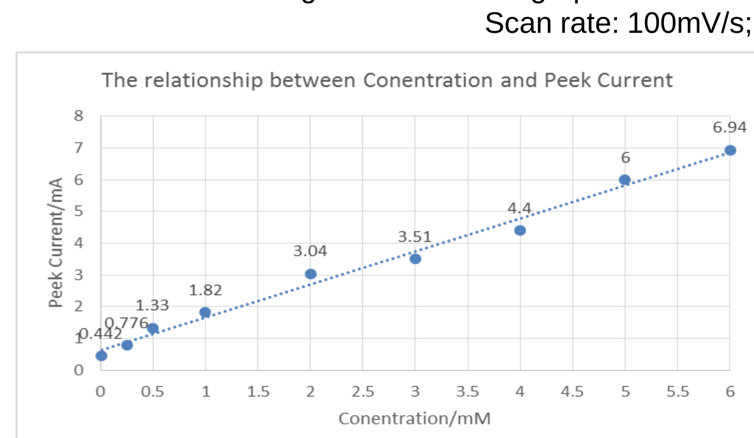


C. Modified by 10 µL graphene dispersion; Deposition time: 480s

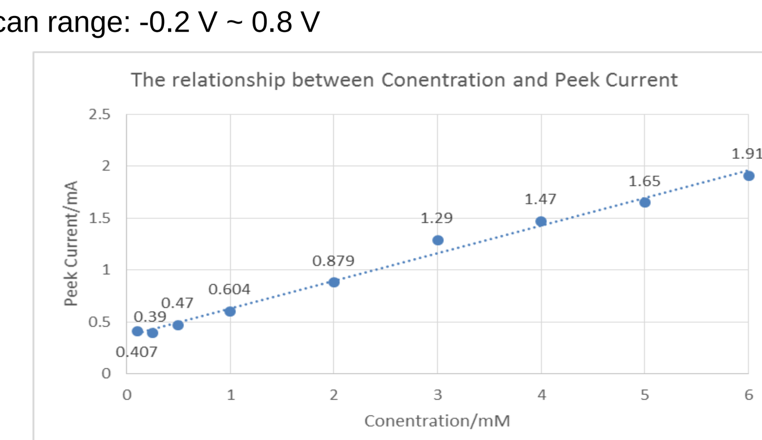


D. Modified by 10 µL graphene dispersion; Deposition time: 1440s

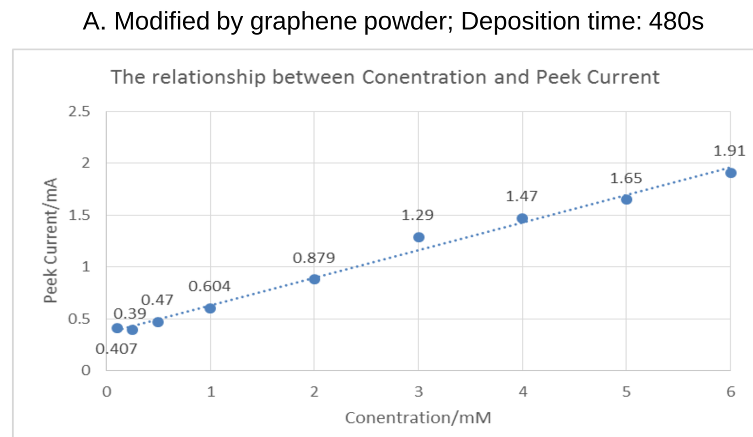
Figure 3. CV of Cu-graphene GC electrode in different concentration of Glucose
Scan rate: 100mV/s; Scan range: -0.2 V ~ 0.8 V



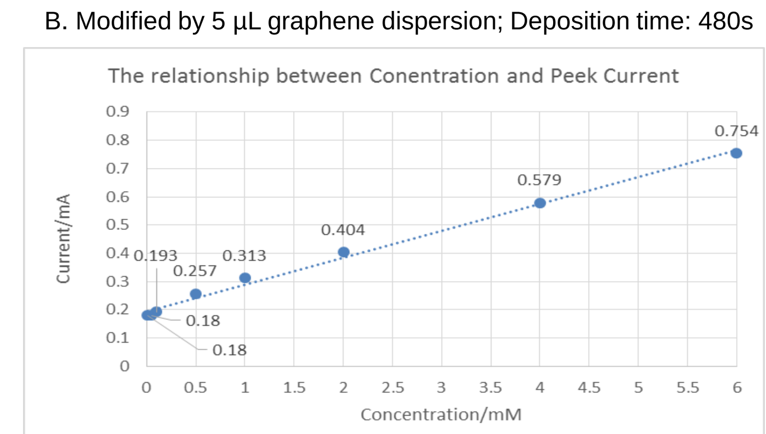
A. Modified by graphene powder; Deposition time: 480s



B. Modified by 5 µL graphene dispersion; Deposition time: 480s



C. Modified by 10 µL graphene dispersion; Deposition time: 480s



D. Modified by 10 µL graphene dispersion; Deposition time: 1440s

Figure 3. The relationship between Glucose concentration and peek current
Scan rate: 100mV/s; Scan range: -0.2 V ~ 0.8 V

According to Figure 3, the Cu-graphene GC electrode showed an irreversible oxidation peek about 0.62V. The electrode modified by graphene powder has the largest peek current. However, graphene sheets on surface of the electrode modified by graphene powder are loose and can be easily peered off. Thus, it results in a poor repeatability. In addition, increasing the deposition time appropriately can increase the peek current. In each case, the peek current value increases regularly when the concentration of glucose increases.

According to Figure 8, peek current is proportional to glucose concentration. The result will guide us on designing the detection system.

Conclusions and Further Work

In the poster, the architecture design of a lab-on-a-chip with graphene-based nanosensor for non-invasive glucose sensing is proposed. So far, the Cu-graphene GC electrode has been modified. The cyclic voltammograms of the electrode by different modified methods and different Cu deposition time in various concentration of Glucose are obtained. The linear relationship between the concentration and the peek current is studied. In the following work, the relationship between the scan rate and the peek current, the effect of PH environment will be discussed. Additional, reproducibility, stability and anti-interference property of the modified electrode are need to be studied.

Acknowledgement

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